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Adenoviral vector carrying glial cell-derived neurotrophic factor for direct gene therapy in comparison with human umbilical cord blood cell-mediated therapy of spinal cord injury in rat

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Abstract

© 2016 International Spinal Cord Society.Study design:Experimental study.Objective:To evaluate the treatment of spinal cord injury with glial cell-derived neurotrophic factor (GDNF) delivered using an adenoviral vector (AdV-GDNF group) in comparison with treatment performed using human umbilical cord blood mononuclear cells (UCB-MCs)-transduced with an adenoviral vector carrying the GDNF gene (UCB-MCs+AdV-GDNF group) in rat.Setting:Kazan, Russian Federation.Methods:We examined the efficacy of AdV-GDNF and UCB-MCs+AdV-GDNF therapy by conducting behavioral tests on the animals and morphometric studies on the spinal cord, performing immunofluorescence analyses on glial cells, investigating the survival and migration potential of UCB-MCs, and evaluating the expression of the recombinant GDNF gene.Results:At the 30th postoperative day, equal positive locomotor recovery was observed after both direct and cell-based GDNF therapy. However, after UCB-MCs-mediated GDNF therapy, the area of preserved tissue and the number of spared myelinated fibers were higher than those measured after direct GDNF gene therapy. Moreover, we observed distinct changes in the populations of glial cells; expression patterns of the specific markers for astrocytes (GFAP, S100B and AQP4), oligodendrocytes (PDGFαR and Cx47) and Schwann cells (P0) differed in various areas of the spinal cord of rats treated with AdV-GDNF and UCB-MCs+AdV-GDNF.Conclusion:The differences detected in the AdV-GDNF and UCB-MCs+AdV-GDNF groups could be partially explained by the action of UCB-MCs. We discuss the insufficiency and the advantages of these two methods of GDNF gene delivery into the spinal cord after traumatic injury.

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